

# Assessment of Changes in Clinical Management of Cervical Cancer Patients in Light of New Staging Criteria

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## Abstract

**Objective:** To assess the changes in the Current clinical management of cancer cervix patients as the new staging considers radiological and pathological criteria for cervical cancer staging.

**Methods:** This retrospective study Retrospective collection of the Data from the medical records.

**Results:** Five hundred and nine Patients were registered for cervical cancer from Jan 2019 to December 2021. The average age of patients treated was 53yrs. The patients' age distribution ( Table 2 ) was Less than one percent of patients below 30yrs, 31.4 percent, and 40.6 percent were in the 50 to 60 yrs range. The parity four patients were nulliparous; the rest were multiparous with one or more deliveries. Patients were staged clinically, radiologically, and surgically. Eleven (2.2%) were stage I and A2, six (1.2%)were IB1, nineteen (3.7%) were IB2, nine (1.8%) were IB3, sixty-one (12%) were stage IIA1, the largest group of the patient were stage IIA2 one thirty-two (26%).and 86(17%). Sixty-seven (13%) were Stage III A, seventy-one (14%) were IIIB, nine(1.6%)were IIIC1, eighteen (3.5%) were IIIC2, eleven (2.3%) were stage IV A, stage IV B were nine(1.7%). The total number of patients diagnosed With squamous cell carcinoma keratinizing was11%and squamous cell carcinoma Nonkeratinizingg 55%. Adenocarcinoma of the cervix and all other histology contributed to 44%. Surgery was performed on 8.2%of patients , 2.2% underwent conization,1.2%underwent simple hysterectomy ,5.1%underwent radical hysterectomy ,and 6%of patients received adjuvant chemoradiation.

**Conclusion:** This study provides the insight into the patients selection for surgical management in early stage cancer cervixIA , IB1,IB2 after clinical and radiological stages. Hopefully, the emphasis on using imaging to measure the tumor size will improve radiological criteria. .patients with stage I B3and more all received Chemoradiation . Further research and well-designed clinical trials are needed for the further clarity on lymph-nodal status, survival outcomes of patientswith new staging.

**Keywords:** FIGO 2018; Cancer Cervix

**Abbreviations:** Concurrent chemoradiotherapy (CCRT); Lymph node metastasis (LNM); magnetic resonance imaging (MRI); computed tomography (CT); fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (PET-CT), SCC -squamous cell carcinoma, SCC NK-squamous cell carcinoma Non-keratinizing, LACC

## Introduction

Cancer staging systems are periodically revised to incorporate new information about prognostic factors Worldwide.

The introduction of New FIGO staging 2018 completely modified the management of the cancer cervix [1-2]. This staging considers the surgical pathological report and radiological imaging [3-4]. The clinical examination are combined to arrive at accurate stage Treatment strategies based on clinical findings. The decision on fertility preservation, the extent of surgery, or consideration of radiation therapy and adjuvant treatment are based on the stage of the disease. In clinical practice, after including the new staging, the Majority of changes are seen in stages IA, IB, and Stage III [5]. Generally, the treatment plan is formulated according to the International Federation of Gynecology and Obstetrics (FIGO) stage. Surgery is reserved for early-stage disease and fertility preservation of smaller lesions, such as stages IA, IB1, and selected IIA1 cases. At the same time, CCRT is generally the primary treatment choice for locally advanced cervical cancer (IB2-IVA stage). Patients with stage IVB disease are treated with systemic chemotherapy [6-8]. The revised staging system requires meticulous and uniform assessment and reporting not only by clinicians but also by pathologists and radiologists

The standard treatment of cervical cancer is stage IB1 to -B2 mainly includes radical hysterectomy and concurrent chemoradiotherapy (CCRT) combined with adjuvant chemotherapy according to the disease. The significant changes in the treatment happened in stage IB3. After the LACC Clinical trial, Minimally invasive surgery For cancer cervix is drastically down. There is no definition of parametrial involvement in the revised

FIGO-2018 staging. Women with microscopic invasion of the parametrium on final histology are allocated to stage IIB, while nodal metastases identified in the parametrium presumably allocate the women to stage IIIC1. It is unknown whether the women with one nodal macrometastasis or Micrometastasis in the parametrium and no positive pelvic nodes share the same survival as women with positive pelvic nodes or should be considered stage IIB [9].

In the FIGO 2018 cervical cancer staging guidelines, patients with positive lymph nodes (LNs) are classified as stage IIIC, irrespective of the tumor size and extent. Disease with pelvic LNM only is considered stage IIIC1, and that with para-aortic LNM is considered stage IIIC2. When LNM was diagnosed by pelvic magnetic resonance imaging (MRI), abdominal computed tomography (CT), (10) or fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (PET-CT) the stage was IIICr, while LNM was IIICp when confirmed by a pathological examination

Lymph node metastasis (LNM) is an independent prognostic factor for progression-free survival (PFS) and overall survival (OS)(11) in early and locally advanced diseases and has been used to help guide postoperative adjuvant therapy in operable early-stage cancer cervix.

The current staging system is only based on the location of LNM. It does not consider the number of LNs, which might limit the accuracy of its prognostic significance to some extent. The LN staging of many other solid tumors usually depends on the location and the number of lymph nodes involved. The presence of LNM greatly influences the prognosis of cervical cancer; survival is also strongly influenced by the extent of the local Tumor. The changes in staging has positive impact on the quality of life and survival of the patient as their treatment is based on current staging.

The study aims to analyze the significant changes in the management after the new FIGO staging ,and the stages where treatment has changed. what would the impact of these changes in their quality of life.

## Methods

This retrospective study conducted at Cancer Insitute WIA, TamilNadu India

The collection of data was retrospectively done from the medical records. The details of Patients who were registered after clinical radiological and pathological cancer cervix diagnosis and treatment.

### Inclusion criteria:

- (i) Newly diagnosed and pathologically confirmed cervical cancer;
- (ii) Staged as IA–IVA based on the FIGO 2018 staging criteria;
- (iii) Treated at the cancer Insitute WIA Chennai from January 2019– December 2021;
- (iv) Treated with surgery or definitive Radiotherapy, chemotherapy, or a combination of surgery and Radiotherapy. Radiotherapy and chemotherapy Cisplatin (30–40mg/m<sup>2</sup> per week) was the first line regimen for concurrent chemotherapy

Adenocarcinomas were classified separately in this study to increase the uniformity of the cohort.

Cervical adenocarcinoma behaves differently from squamous cell carcinoma in terms of disease progression pattern and response to treatment. The proportion of adenocarcinoma among all cervical cancer cases differs by FIGO stage.

The institutional Research board and ethical review committee approved this study.

For staging, the patients received the following examinations: (a) bimanual pelvic examination,

(b) cystoscopy if indicated, (c) colonoscopy if indicated, (d) CT from the upper abdomen to the pelvis, (e) MRI of the abdomen pelvis, and (f) The FDG-PET whole body was done if patients were found to have stage IV b disease. All the pre-treatment examinations were performed.

The FIGO 2018 staging used the findings from Notation for stage IIIC as stage IIICr in all patients.

## Results

The 2018 FIGO system (Table 1) describes the age.

A total of 509 patients were registered for cervical cancer from Jan 2019 to December 2021. The average age of patients treated was 53yrs. The age distribution (Table 2) of the patients were Less than one percent of patients were below 30yrs, 31.4 percent were, and 40.6 percent were in the 50 to 60 yrs range.

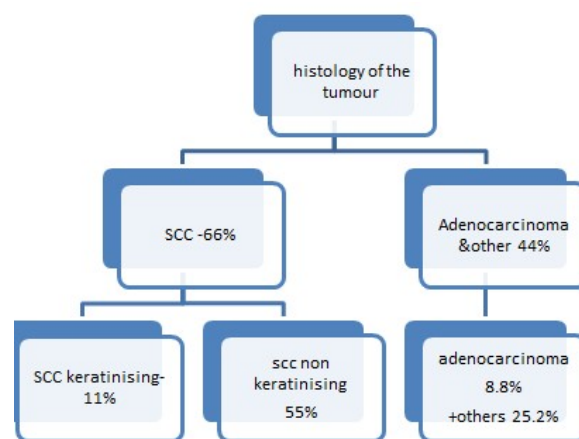
**Table 1:** Baseline Characteristics Age

Demographics		
Age of patients(years)	Number of patients	percentage
<30	4	0.7%
31 to 40	46	9.0%
41 to 50	160	31.4%
51 to 60	207	40.6%
61 to 70	83	16.3%
>71	9	1.7%
Nulliparous	4	0.7%
Multiparous	505	99.3%

The parity four patients were nulliparous, and the rest were multiparous with one or more deliveries.

**Table 2**

Demographics		
Age in years	Median range	52 (35-71)
Comorbid illness	Absent/present	217/292
Performance status	0,1/2,3	331/178
Family history of malignancy	Absent/present	468/41
BMI	< 18/ > 18	387/122
Menopausal status	Premenopausal/postmenopausal	157/352
Stage at diagnosis	Early stage I,II/III,IV	
Tumour histology	SCC/adenocarcinomas & others	338/171



**Figure 1**

The total number of patients diagnosed with squamous cell carcinoma keratinising were 11% and squamous cell carcinoma non-keratinising 55%. Adenocarcinoma of cervix and all other histology contributed to 44%. The histopathological diagnosis was mostly by biopsies.

**Table 3:** Histology of Tumour

Type of Carcinoma	No of Patients	Percent %
Squamous cell carcinoma	56	%
Squamous cell carcinoma - Non-Keratinising	280	55.01
Adeno Carcinoma	45	8.84
Adeno Squamous carcinoma	14	2.75
Basiloid Squamous carcinoma	2	0.39
Carcino sarcoma	2	0.39
Neuro Endocrine Carcinoma	6	1.18
Epidermoid Carcinoma	84	16.50
mucionous adeno carcinoma	2	0.39
Unclassified carcinoma	9	1.77
Total	509	100

**Table 4:** Stages of Cervical Cancer

Stage of Cancer Cervix	Number	Percent %
Stgae 1A1 and A2	11	2.2
Stage 1B1	6	1.2
Stage 1B2	19	3.7
Stage 1B3	9	1.8
Stage IIA1	61	12
Stage IIA2	132	26
Stage IIA2	86	17
Stage IIIA	67	13
Stage IIIB	71	14
Stage IIIC1	9	1.6
Stage IIIC2	18	3.5
Stage IV A	11	2.3
Stage IVB	9	1.7

Patients were staged clinically, radiologically, and surgically. Eleven (2.2%) were stage I and A2, six (1.2%) were IB1, nineteen (3.7%) were IB2, nine (1.8%) were IB3, sixty-one (12%) were stage IIA1, the largest group of the patient were stage IIA2 one thirty-two (26%).and 86(17%). Sixty-seven (13%) were Stage III A, seventy-one (14%) were IIIB, nine(1.6%)were IIIC1, eighteen (3.5%) were IIIC2, eleven (2.3%) were stage IV A, stage IV B were nine(1.7%).

Treatment	Percent
Surgery	2.2
Surgery and adjuvant ChemoRT	4.1
Radiotherapy	63.8
Chemoradiotherapy	23.9
Chemotherapy	2.4
Palliative treatment	1.7
Surgery and RT	1.9

**Table 5:** Management of the Disease.

The patients with early stage Surgery was performed on 8.2% of patients- eleven 2.2% underwent conisation ,1.2% underwent simple hysterectomy ,5.1% underwent radical hysterectomy and 6% of patients received adjuvant chemoradiation.

As per new staging the number of patients undergoing surgical management was reduced significantly and stage IIIc1 nad IIIC2 which was not in older classification had significant number.

## Discussion

The 2018 FIGO revision for cervical cancer staging offers a more extensive assessment of the Tumor by more accurately determining disease spread, prognosis, and vital information for treatment planning. Stage I disease is divided into two categories, IA and IB.

Stage IAs are only visualized with microscopy. Stage IA has changes that guide the extent of surgical management fertility preservation. 4 cm were classified as stage IB2. In the revised system, substages for stage IB disease increase every 2 cm increments in tumor size: stage IB1 (<2 cm), stage IB2 disease (2 cm to <4 cm), and stage IB3 ( $\geq$ 4 cm). Previously designated stage IB1 disease is now further subdivided into 2 groups in the new staging system. Notably, tumor size of >4 cm was staged as IB2 in the former system, and tumor size  $\geq$ 4 cm is stage IB3 in the updated system.

Based upon a recent validation analyses of Matsuo et al. [2] using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program between 1988–2014, the revised FIGO staging system for cervical cancer is useful to distinguish survival groups [12]. Applying the new system, stage IB1 and stage IB2 disease have distinct characteristics and outcomes, e.g., stage IB1 disease is more likely to be low-grade, and have adenocarcinoma histology, whereas stage IB2 disease is more likely to be high-grade and have squamous histology. Patients with stage IB2 disease are more likely to undergo pelvic lymphadenectomy and radical hysterectomy, while women with stage IB1 disease are less likely to have received postoperative radiotherapy. Additionally, patients with stage IB2 disease have a nearly 2-fold increased risk of cervical cancer death compared to those with stage IB1 disease. Based on this new classification, risk-stratification will be very useful when applied to the treatment algorithm for tumors less than 4 cm.

There are several key clinical implications of the FIGO 2018 staging. Fertility-sparing trachelectomy is an acceptable operation for stage IB1 disease, but not stage for IB2 disease as per the National Comprehensive Cancer Network guidelines [13].

Stage IA disease no longer includes horizontal spread and now only relies on the depth of invasion. The depth of invasion is a more significant predictor of survival than horizontal spread because it is a better predictor of recurrence and lymph node metastasis. Furthermore, the staging is based on the depth of stromal invasion and the largest size of measured cancer. In our study, there was very scanty histopathological differentiation for correctly classifying stage IA1.

Stage IB had more radical changes than stage IA. Any terminology related to the clinical visibility of the Tumor automatically becomes Stage IB. Dividing women with stage IB into three sub-stages (IB1, IB2, and IB3) improved prognostic discrimination. An increased discriminatory ability within IB tumors was also a finding of Grigsby et al. [14]. Furthermore, there are now three sub-stages instead of two of stage IB. Previously, stage IB1 included cervical masses smaller than 4 cm in greatest diameter. Patients who were previously stage IB2

In the revised staging system, stage IB1 is split into two stages: tumors lesser than 2 cm (IB1), equal to or larger than 2 cm, but lesser than 4 cm (IB2). The third substage (IB3) newly added includes tumors larger than 4 cm in the most significant dimensions.

The other sub-staging of IB1 is based on evidence that patients with tumors lesser than 2 cm in diameter have a better outcome than patients with tumors measuring 2–4 cm. stage I B with Tumor size more than 4 cm is stage IB3 is a new substage in the new classification. This stage has the maximum impact on the therapeutic management of cervical cancer. The Majority of stage I B3 are treated with chemo-radiation. Stage II did not have any modifications from the previous FIGO classification. Therefore no changes in stage II management.

In the previous FIGO staging system, lymph node metastasis did not have a role in staging. There is the new addition of stage IIIC in FIGO staging 2018.

Stage IIIC is any cervical cancer with pelvic lymph node involvement is sub staged into stage IIIC1, and with pelvic nodes, The paraaortic nodal involvement with or without pelvic nodes is substage as IIIC2, irrespective of tumor size and the local invasion to adjacent structure [15]. Involvement of paraaortic lymph nodes leads to a worse prognosis than pelvic lymph node involvement. Patients with pelvic lymph node metastasis have a 5-year survival rate of less than 50%, whereas lymph node metastasis of paraortic node survival is less than 20–30% [16].

The evaluation of nodal status can therefore have a tremendous impact in the treatment planning with Radiotherapy. For example, the presence of metastatic lymph nodes in the pelvis or para-aortic area can lead to plan an intensity-modulated radiation therapy (IMRT)-integrated boost with dose escalation on that involved area [17]. In the era of image-guided adaptive Radiotherapy, accurately defining disease areas is critical to avoid irradiating normal tissue. Based on additional information provided by CT/MRI, radiation treatment volumes can be modified and higher doses to positive lymph nodes safely delivered.

Improvements in tumor staging by imaging modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), and fluorine-18-labeled fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) can significantly improve treatment decisions and the accuracy of highly precise treatment modalities like fertility preserving surgeries (If needed) for stage IA and IB1, radical surgeries and definitive radiotherapy treatment planning.

Patient age, clinical stage, histologic type, histologic grade, tumor size, metastases to the lymph nodes, lymphovascular space invasion, and the condition of the surgical margins after surgery defines the prognosis of the patient [18]. These factors were taken into consideration before planning for radiation therapy. The external beam radiotherapy of 45–50.4 Gy was delivered by the four-field technique using linear accelerators or by tomotherapy. Prophylactic extended field radiotherapy covering the PAN region was applied to the patients. An additional 10–20 Gy boost was given to the positive pelvic nodes > 1.5 cm in diameter at diagnosis, according to the institutional policy. High-dose-rate brachytherapy with a median physical dose of 30 Gy in 3-4 fractions was delivered once a week. Weekly cisplatin was given concurrently with Radiotherapy. Hysterectomy was performed with the Piver–Rutledge type 2 or 3 combined pelvic lymphadenectomy using either laparotomy or laparoscopy. After the surgery, tailored adjuvant therapy was administered to patients with a high-risk pathologic factor or two or more of the intermediate-risk features. Adjuvant external beam radiotherapy was delivered to a total 46 Gy–50.4 Gy dose. Vaginal stump brachytherapy was considered for patients with positive or close vaginal margins after the completion of external Radiotherapy. In patients, two to four sessions of the high-dose-rate brachytherapy were delivered once every week, with a fractional dose of 5–6 Gy.

Approximately 90% of the cases were eligible only to Radiotherapy or concurrent chemotherapy. Only early stage Ca cervix who were managed by surgery was only 5.4% from these 1.7 % needed adjuvant Radiotherapy. Epidemiological study of the revised staging system with applying pooled national dataset is required to have the correct and valuable judgment and guidance [19-20]. weakness of the study is retrospective nature, prognosis and survival analysis are not included.

## Conclusion

This study provides the insight into the patients selection for surgical management in early stage cancer cervix IA , IB1,1B2 after clinical and radiological stages. Hopefully, the emphasis on the use of imaging to measure the tumor size will lead to improved radiological criteria. The patients selection for surgery is reduced due to the involvement of radiological lymph nodes. Patients with stage I B3 and more all received Chemoradiation . Further research and well-designed clinical trials are needed for the further clarity on lymph-nodal status, survival outcomes of patients with new staging.

## Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper

## Author Contributions

All authors contributed to the manuscript at all stages including design, planning, data abstraction, and manuscript writing.

## Ethical Approval

Obtained from the Institute review board.



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